

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 35-72 are pending in the application, with claim 35 being the sole independent claim. Claims 1-34 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 35-72 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***I. Support for New Claims***

Support for new claim 35 can be found, for example, in the specification at page 7, line 18 through page 8, line 13, at page 10, line 25 through page 11, line 6, at page 14, line 15 through page 15, line 8, and in original claims 1, 2, 6, 15 and 17.

Support for new claims 36-38 can be found, for example, in the specification at page 7, lines 12-17, and in original claims 3-5, respectively.

Support for new claims 39 and 40 can be found, for example, in the specification at page 8, line 24 through page 9, line 2, and in original claim 16.

Support for new claims 41 and 42 can be found, for example, in the specification at page 8, lines 3-23.

Support for new claims 43-45 can be found, for example, in the specification at page 7, lines 18-21.

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Support for new claims 46-49 can be found, for example, in the specification at page 10, line 25 through page 13, line 27.

Support for new claims 50-53 can be found, for example, in the specification at page 13, line 28 through page 14, line 14, and in original claim 21.

Support for new claim 54 can be found, for example, in the specification at page 14, line 28 through page 15, line 8, and in original claim 22.

Support for new claims 55 and 56 can be found, for example, in the specification at page 14, lines 15-27 and in original claims 7-10, 25 and 26.

Support for new claim 57 can be found, for example, in the specification at page 15, lines 2-5.

Support for new claim 58 can be found, for example, in the specification at page 15, line 27 through page 16, line 3.

Support for new claims 59-62 can be found, for example, in the specification at page 16, lines 15-23, and in original claims 12-14.

Support for new claims 63 and 64 can be found, for example, in the specification at page 14, lines 15-17, and in original claims 23 and 24.

Support for new claims 65-67 can be found, for example, in the specification at page 14, lines 15-27 and in original claims 11, 27 and 28.

Support for new claims 68-70 can be found, for example, in the specification at page 15, lines 9-26, and in original claims 30-32.

Support for new claims 71 and 72 can be found, for example, in the specification at page 16, line 24, thorough page 17, line 5, and in original claims 33 and 34.

**II. Examiner Interview**

Applicants and Applicants' undersigned representative thank the Examiner for the Examiner Interview conducted on May 16, 2002 in which the rejection of claims 1-34 under 35 U.S.C. § 102 was discussed.

**III. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-34 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Paper No. 18, page 2. Applicants respectfully traverse this rejection.

This rejection is directed specifically to the phrase "the nucleotide compositions of  $(X_1X_2)_n$  and  $(Y_1Y_2)_n$  are substantially identical," in claim 1, and to the phrase "the nucleotide compositions of  $(X_1X_2)_nA_m$  and  $B_m(Y_1Y_2)_n$  are substantially identical," in claim 2. According to the Examiner, "it is not clear whether the claimed nucleotides are to be compared for substantial identity between the strands or between nucleotides of a particular strand. . ." *See* Paper No. 18, page 3.

Applicants respectfully submit that the intended meaning of the two phrases in question would be clearly understood by those of ordinary skill in the art, especially in view of the specification which states:

[b]y "substantially identical in base composition" is meant that the top and bottom strands of the repeat-containing sequence are about 80%, preferably at least about 90%, more preferably at least about 95%, still more preferably at least about 98% or about 99%, and most preferably at least about 100%, identical in base composition.

See specification at page 8, lines 7-11.

Moreover, as understood by persons of ordinary skill in the art, the term "base composition" refers to the relative proportion of each nucleotide base (A, C, G and T) in a given nucleotide sequence. It is clear, therefore, that the substantial identity referred to in claims 1 and 2 is between the top and bottom strands of the recited repeat-containing sequences. Thus, the intended meaning of *nucleotide compositions that are substantially identical* is that, in a double stranded nucleic acid molecule, the percentage of each nucleotide in one strand of the molecule is substantially the same as the percentage of each respective nucleotide in the opposite, complementary, strand of the molecule.

Solely to make explicit the implicit meaning of the phrases recited in claims 1 and 2, these claims have been cancelled and new claim 35 has been added. Claim 35 includes the expression ". . . wherein the top strand of said repeat-containing sequence has substantially the same percentage of each respective nucleotide as in the bottom strand. . ." Applicants respectfully submit that this expression would be clearly understood by persons of ordinary skill in the art. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, has been fully accommodated and should be withdrawn.

#### **IV. Claim Rejections Under 35 U.S.C. § 102**

Claims 1-21 and 23-34 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,824,787 to Singer (hereinafter "Singer"). Applicants respectfully traverse this rejection.

Under 35 USC § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. See *Kalman v. Kimberly*

*Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984); *see also PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996) ("[t]o anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.") Since Singer does not teach or suggest all of the elements of any of Applicants' claims, Singer cannot and does not anticipate Applicants' claims.

Claims 1-21 and 23-34 have been cancelled. Claims 35-72 have been added to make explicit the subject matter that Applicants originally intended to be encompassed by claims 1-34. New claims 35-72 are directed to, or include the use of, nucleic acid molecules comprising two or more copies of a repeat-containing sequence. As recited in new claim 35, "said repeat-containing sequence is a double-stranded polynucleotide having from about 5 to about 1000 base pairs, and wherein the top strand of said repeat-containing sequence has substantially the same percentage of each respective nucleotide as in the bottom strand." *See also* specification at page 8, lines 1-5 and the exemplary repeat-containing sequences listed on page 8, lines 16-23.

The molecules in Singer do not contain a "repeat-containing sequence," as this term is defined in Applicants' specification and claims. In particular, the sequences listed in Singer, Table 1, when made double stranded, would not form polynucleotides wherein the top strand has substantially the same percentage of each respective nucleotide as in the bottom strand (*i.e.*, the top and bottom strands of the sequences in Singer would not have "substantially identical base compositions.") For example, the sequence element designated "EP/SmP" in Singer has the following (top strand) nucleotide sequence:

GTT GTG TGG GGG GTT TTT AG.

In double-stranded form, the complementary (bottom) strand of EP/SmP would have the following sequence:

CAA CAC ACC CCC CAA AAA TC.

The base composition of the top strand is: 5% A, 0% C, 50% G and 45% T. The base composition of the bottom strand is 45% A, 5% C, 0% G and 5% T. Thus, the sequence designated EP/SmP in Singer, in double-stranded form, does not have substantially the same percentage of each respective nucleotide in the top strand as in the bottom strand. In fact, the base compositions of the two strands are completely different from one another.

By contrast, the repeat-containing sequences that are included within the present claims have substantially the same percentage of each respective nucleotide in the top strand as in the bottom strand. In fact, the exemplary repeat-containing sequences set forth in the specification at page 8 exhibit *identical* top and bottom strand base compositions. For example, SEQ ID NO:1 (ATC TCA GGA T) has the following base composition: 30% A, 20% C, 20% G and 30% T. The complementary (bottom) strand (TAG AGT CCT A) has the *same* base composition, that is, 30% A, 20% C, 20% G and 30% T. In other words, the repeat-containing sequence designated as SEQ ID NO:1 has the same percentage of each respective nucleotide (A, C, G and T) in the top strand as in its bottom (complementary) strand. As the specification makes clear, this identity of base composition is of great significance, for example, in determining the manner in which the top and bottom strands migrate relative to one another on polyacrylamide gels. *See* specification at page 16, lines 4-11.

Singer fails to expressly or inherently disclose every element of Applicants' claimed invention. Applicants therefore respectfully submit that the rejection of claims 1-21 and 23-

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34 under 35 USC § 102(e) was improper and, accordingly, should not be applied to new claims 35-72.

#### ***V. Claim Objections***

The Examiner objected to claim 22 as being dependent upon a rejected base claim. See Paper No. 18, page 4. The Examiner stated that claim 22 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. See *id.*

Applicants note that claim 22 has been cancelled; however, the subject matter encompassed by claim 22 is now encompassed by new claim 54. As discussed in detail above, the rejection under § 102(e) was improper and should not be applied to the presently presented claims. Accordingly, the objection to claim 22 as being dependent upon a rejected base claim was likewise improper and should not be applied to new claim 54.

#### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite

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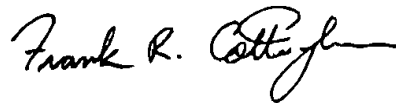
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prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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**Version with markings to show changes made**

Claims 1-34 are sought to be cancelled without prejudice or disclaimer.

New claims 35-72 are sought to be added.

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To: U.S. Patent and Trademark Office

Date: January 29, 2003

Attention: Examiner Jane Zara  
Group Art Unit 1635Re: U.S. Utility Patent Application  
Appl. No. 09/472,067; Filed: December 23, 1999  
For: Nucleic Acid Ladders  
Inventors: HU *et al.*

From: Frank R. Cottingham (FRC)

Pages (including cover sheet): 20

Our Ref: 0942.4340002/RWE/FRC

Fax No: (703) 308-4242

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## Message

Transmitted herewith for appropriate action are the following documents:

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2. Supplemental Amendment And Reply; and
3. Facsimile Cover Sheet.

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January 29, 2003

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*Via Facsimile to  
Examiner Jane Zara  
Art Unit 1635*

Re: U.S. Utility Patent Application  
Appl. No. 09/472,067; Filed: December 23, 1999  
For: **Nucleic Acid Ladders**  
Inventors: HU *et al.*  
Our Ref: 0942.4340002/RWE/FRC

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Supplemental Amendment And Reply; and
2. Facsimile Cover Sheet.

It is respectfully requested that the attached facsimile cover sheet be stamped with the date of filing of these documents, and that it be returned to us by via facsimile. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents

January 29, 2003

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Respectfully submitted,

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Enclosures

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